Remarks:

Regarding the rejection of claims 1-4, 12-15 and 17-21 under 35 USC 102(b) in view of US 4678658 to Casey et al. (hereinafter "Casey"):

The applicant traverses the rejection of the claims in view of the reference to Casey, particularly in view of the foregoing amendments to the claims. .

With regard to the Examiner's grounds of rejection under 35 USC §102(b), that statute holds in relevant part that a person shall be entitled to a patent unless "the invention was ... in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States." Unpatentability based on "anticipation" requires that the invention is not in fact new. See *Hoover Group, Inc. v. Custom Metalcraft, Inc.*, 66 F.3d 299, 302, 36 USPQ2d 1101, 1103 (Fed. Cir. 1995) ("lack of novelty (often called 'anticipation') requires that the same invention, including each element and limitation of the claims, was known or used by others before it was invented by the patentee"). Anticipation requires that a single reference describe the claimed invention with sufficient precision and detail to establish that the subject matter existed in the prior art. See, *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990). It is the present applicants' position that this standard has not been met.

Regarding now the Casey reference, a skilled artisan reviewing that document would understand that the invention disclosed by Casey are to compositions are also distinguishable from the presently claimed compositions. More specifically, whereas the applicant's three essential constituents are: water, a selected alcohol from a defined group and a pH adjusting agent, the compositions according to Casey necessarily include: an

> "..aliphatic alcohol with high volatility is used as the primary component by volume. The alcohol has bactericidal characteristics and allows for the rapid drying of the layer of disinfectant sprayed on the surface..." (Casey, column 2, lines 17 – 22);

The Casey compositions however also necessarily require a "germicide-surfactant" which is discussed in Casey as follows:

> "It is thought that the surfactant has two characteristics which contribute to this invention. Those being germicidal activity including effectiveness over a wide range of organisms including bacteria, virus and yeast and providing a reduction of the surface tension of the composition to achieve effective spread and distribution if the germicide on the surface is to be disinfected. Two different types of surfactants were tested separately and in combination for efficacy. It was found that both sodium dodecyl sulfonate and octyl phenoxy polyethoxyethanol are effective germicide-surfactants. There are other compounds which have the properties of germicide-surfactants, and this invention is not limited to those compounds shown in the examples." (Casey, col. 2, lines 37 – 50);

From the foregoing it is believed to be quite apparent that the Casey compositions do not anticipate or suggest the present applicant's compositions.

The Casey reference clearly teaches that the efficacy against microorganisms is achieved by the effect of both the large amount of alcohol necessarily present in conjunction with the "surfactant-detergent compounds" a mechanism which appears to be quite different from the "essential ingredients" which are essential to the present applicant's invention. There is no recitation in Casey with regards to any criticality respecting any specific combination of specific pH level and specific level of alcohol, nor for that matter, any specific and surprising inverse relationship between the pH level and the level of specific alcohol(s) present in the composition in order to achieve any kill against the polio virus. Furthermore, the Casey reference fails to disclose a system which is based only on the "essential constituents" which the present applicant teaches in their application. Casey can be contrasted in that while it does provide some degree of antimicrobial efficacy, the required constituents according to Casey are distinguishable from the applicant's

"essential constituents" and thus the applicant's present claims should be considered as novel over the Casey reference.

The Casey reference also fails to teach compositions which are based on anything other than 70%wt. isopropanol and 30% wt. water mixtures. (See Casey, col. 2, lines 26 – 29.) Thus Casey fails to suggest or demonstrate efficacy of his compositions at any lesser amount of alcohol being present.. That good overall efficacy can be attained at 70%wt. or greater amounts of alcohol being present is well known to the art; see the present application at page 1, lines 26 – 28 wherein this effect is discussed by the applicant as background to the present invention. Thus, Casey does not teach efficacy against poliovirus type 1 at anything but such high concentrations of alcohol which was known to the art.

The Casey reference also fails to teach any relationship between the amount of alcohol which may be present or the pH of the composition. Such is a dual failure as Casey fails to demonstrate any variability in the amount of isopropanol which may be used, and fails to demonstrate efficacy at compositions other than at a pH of 12.53. From Casey's Examples I, II and III it appears that all testing was done using an example composition which had a pH of 12.53 (see Casey, column 3, lines 57 – 58). Thus, no variability in the pH of the compositions and potential effect on microorganisms was disclosed either.

The applicant also points out that Casey's demonstrated efficacy is against a short list of microorganisms as outlined by Casey at col. 1, lines 53 – 58. As is known to a skilled practitioner in the arts, antimicrobial efficacy is not necessarily inherent or easily predictable against other types of microorganism, even of the same genus. Thus, it is also fair to say that Casey fails to demonstrate any efficacy of his microorganisms against those enumerated in the previously presented claim 22, namely *Salmonella choleraesuis*, *Pseudomonas aeruginosa*, *Entercoccus hirae* , *Aspergillus niger*, *T. mentagrophytes*, Hepatitis A , Poliovirus Type 1, Coxsachievirus , Rotavirus, or Rhinovirus. It is particularly fair to say that Casey fails to demonstrate any efficacy against Poliovirus

Type 1 which is demonstrated by the present applicants, but not at all described by Casey.

The applicant notes that Casey recites at col. 4 lines 1 – 8 the following microorganisms

4

This composition was tested for germicide effectiveness against *Herpes simplex* virus type 2 (HSV2), *Neisseria gonorrhoeae*, *Staphylococcus aureus*, *Escherichia coli* 011K58, *Shigella sonnei*, *Salmonella typhimurium*, and *Candida albicans*. The composition was sprayed and dropped on pathogen suspensions to test efficacy and dye color disappearance.

And later at col. 5, at "Table 1" Casey illustrates the results of testing on those microorganisms

4,5 / 5,1

5

TABLE I

The Microcidal Activity of Example I Against Various Pathogens

Pathogen	No. of tests	Mean Percent killing	Range	Comments
S. aureus	6	>99*	99-99.9	Similar killing by drop or spray.
C. albicans	6	>99	99-99.9	Similar killing by drop or spray.
N. gonorrhoeae	3	>99	99-99.9	Similar killing by drop or spray.
E. coli 011K58	3	>99	99-99.9	Similar killing by drop or spray.
S. sonnei	3	>99	99-99.9	Similar killing by drop or spray.
S. typhimurium	3	>99	99-99.9	Similar killing by drop or spray.
HSV2	6	99	99-99	Similar killing by drop or spray; may be > than 99% killing but toxicity of Example I to VERO cells made lower dilutions unreadable.

*Percent killing was determined by dividing the total number of viable organisms in suspensions exposed to Example I by the total number of viable organisms in suspensions exposed to phosphate buffered saline and multiplying by 100.

against a formulation which is described as "Example 1" at col. 3, lines 47 – 57.

EXAMPLE I

A sample of the germicidal composition was prepared by adding 400 mg of sodium dodecyl sulfate (SDS) and 400 of octyl phenoxy polyethoxyethanol marketed as Triton X-100 a product of Sigma Chemical Company to 100 ml of 70% by volume isopropanol. 100 mg of blue dye thymophthalein was added. The pH was adjusted with 0.05 ml of 12N NaOH which produces a deep blue colored liquid when keep air tight. This also gave a pH of 12.53 to the liquid. When the composition

The formulation can be seen to comprise approximately 70%wt. isopropanol, and has a pH of 12.53.

The applicant notes that the described efficacy against the microorganisms recited on Table 1 of Casey does not anticipate, nor for that matter render as 'obvious' the applicant's presently claimed invention. As is currently claimed in claim 1, 22 and in particularly claim 23 the applicant's compositions demonstrate efficacy against organisms which are recognized in the art as being substantially more difficult to eradicate then the microorganisms demonstrated by Casey.

The applicant notes that to a skilled artisan, that microorganisms are usually classified with regard to their durability and resistance to eradication and several well recognized scales exist. Two are provided as attachments to this paper. With reference first to page 548 of the widely recognized textbook "Disinfection, Sterilization and Preservation" 5th. Ed. Seymour S. Block, PhD (Editor) (2001) provides at "Table 28.5 an 'approximate disinfection scale for all organisms in order of increasing resistance' which ranks classes of microorganisms from the least resistant as group "A", and in order of rapidly increasing increasing resistance to eradication to group "G". Representative organisms for each of the groups in Table 28.5 are provided. Now with reference to Table 1 of Carey it would be recognized that each of *S. aureus, C. albicans, N. gonorrhoeae, E. coli, S. sonnei and S. typimurium* would be recognized as being a group "B" type microorganism, an only slightly more resistant to eradication than group "A" type microorganisms which include Casey's HSV2 from his Table 1. It is particularly relevant

to note that the microorganisms claimed in applicant's claims are of more difficult to eradicate classes. Particular attention should be made of the fact that rotaviruses are of group "D" and polio viruses and rhinovirus are even more difficult to eradicate as they are classed as group "E" on the Table 28.5 scale.

The second document, a paper approved for publication shortly in the *Infection Control and Hospital Epidemiology Journal* titled "Should the Test Methods for Efficacy of Disinfectants use Vertebrate Viruses Dried on Carriers to Advance Virucidal Claims Substantiation in Public Health Arena", by Dr. M. Khalid Ijaz and Joseph Rubino includes a table also ranking various microorganisms and their resistance to microbiocides. The table is reproduced here:

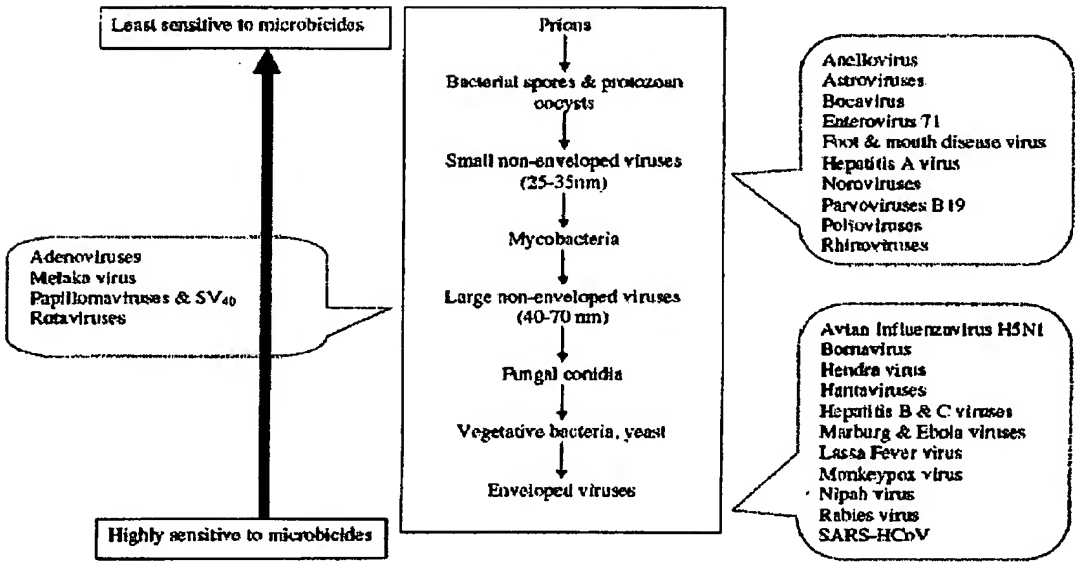

Figure : Emerging / re-emerging viruses and microbicidal hierarchy.

Again, it is pointed out that a skilled artisan considering Table 1 of Casey would identify that each of *S. aureus, C. albicans, N. gonorrhoeae, E. coli, S. sonnei and S. typimurium* would be recognized as being in the class of "vegetative bacteria, yeast" of the above

chart, and that Casey's HSV2 would be even easier to eradicate as being an "enveloped virus." In harsh contrast , as is also seen on the above chart polioviruses and rhinoviruses are recognized as being much more resistant to eradication.

Additionally the applicant directs the Examiner's attention to claims 16 and 21 wherein ethanol is indicated as being the sole alcohol constituent present in the compositions. The applicant notes that such formulations are fully supported by applicant's Examples 69 - 101 which include ethanol as the sole alcohol constituent present. The applicant notes that none of Casey's two compositions include ethanol, rather include isopropanol as an alcohol in the absence of ethanol.

The applicant also points out that the claimed compositions demonstrate anti-fungal efficacy as they are effective against fungal spores of *Aspergillis niger*. Casey in no way indicates or suggests efficacy against fungal spores, which are however known to a skilled artisan in the relevant art to be much more resistant to eradiction than the species identified in Casey's Table 1.

The applicant notes that the further example composition provided by Casey at "Table 5" is provided with no demonstrated antimicrobial efficacy but appears to be merely provided to demonstrate that Casey's compositions may be pressurized. As the composition of Table 5 has a substantially reduced amount (51.62%wt.) isopropanol, one of skill in the art would not draw any conclusions or expect any antimicrobial efficacy even comparable to Casey's "Table 1" composition comprising the significantly higher amount (about 70%) of isopropanol.

Accordingly, in view of the foregoing remarks, reconsideration of the propriety of the rejection under 35 USC 102(b) is requested, and it is further requested that the rejection be withdrawn.

Regarding the rejection of claims 5-7, and 16 and 22 under 35 USC 103(a) over US 4678658 to Casey in view of EP 0099209 to Coates (hereinafter "Coates"):
The applicant respectfully traverses the rejection of claims 5-7 and 16 in view of the combined Casey and Coates references.

For the sake of brevity, the applicant herein repeats and incorporates by reference all of the foregoing remarks concerning the Casey reference as being equally applicable with regard to the instant grounds of rejection.

With respect to the Coates reference, Coates recites at page 2 -3:

"According to the present invention, an aqueous disinfectant solution comprises:

a) 60 to 80% w/w of a C_1 to C_4 alkanol;

b) a bisguanide antimicrobial agent; and

c) a quaternary ammonium antimicrobial agent, wherein the combined concentration of the antimicrobial agents in the solution is up to 2% w/v.

Preferably the combined concentration of the antimicrobial agents in the solution is up to 2% w/v."

Coates later recites at page 4:

"The composition may also include a chelating agent, such as ethylenediaminetetra-acetic acid (EDTA), which are known to render some micro-organisms more susceptible to antimicrobial agents."

From the foregoing it is believed to be quite apparent that the Coates compositions do not anticipate or suggest the present applicant's compositions, nor would they render the currently claimed compositions obvious if considered in conjunction with the Casey reference. Coates clearly teaches that the efficacy against microorganisms is achieved by the combination of the bisguanide antimicrobial agent with the quaternary ammonium

antimicrobial agent. There is no recitation in Coates respecting any criticality respecting any specific combination of specific pH level and specific level of alcohol in achieving any kill any microorganism, particularly polio virus and other microorganisms which the applicant now claims in prior presented claim 22, and particularly in newly presented claim 23. Although Coates suggests that EDTA may improve the efficacy of antimicrobial agents, when read in the context of the Coates specification, such would be limited to the combination of the bisguanide antimicrobial agent with the quaternary ammonium antimicrobial agents taught. In any case, again, nothing in Coates provides any teaching or exemplification of the criticality of any specific combinations of specific pH level and specific level of alcohol in achieving any kill any microorganism, particularly the polio virus. The compositions in the Coates are demonstrated only against *Pseudomonas aeruginosa, Staph. aureus, Escheria coli, and Salmonella choleraeusis*. For the sake of brevity, the applicant notes again that microorganisms of the Coates reference are again of the group "B" type discussed above and are far easier to eradicate than at least poliovirus and the other types of microorganisms now claimed. Thus, Coates does not teach or suggest, nor provides any motivation, nor raises any expectation that combining Coates with Casey would provide any improvements to antimicrobial efficacy of either the Coates or Casey compositions considered jointly or severally.

Additionally, with respect to rejections lodged under 35 USC 103(a), the Examiner is reminded that there should be some suggestion, teaching, or motivation arising from what the prior art would have taught a person of ordinary skill in the field of the invention to make the proposed changes to the reference. *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988). It must also be shown that one having ordinary skill in the art would reasonably have expected any proposed changes to a prior art reference would have been successful. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207, 18 USPQ2d 1016, 1022 (Fed. Cir. 1991); *In re O'Farrell*, 853 F.2d 894, 903-04, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); *In re Clinton*, 527 F.2d 1226, 1228, 188 USPQ 365, 367 (CCPA 1976). "Both the suggestion and the expectation of success must be

founded in the prior art, not in the applicant's disclosure." *In re Dow Chem. Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). With regard to such a suggestion the Courts have also clearly stated it is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to "[use] that which the inventor taught against its teacher." *W.L. Gore*, 721 F.2d at 1553. Only by insisting upon this rigor can the court avoid entry into the "tempting but forbidden zone of hindsight," *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 873 [228 USPQ 90] (Fed. Cir. 1985). It is not believed that the Examiner's current rejection under 35 USC 103(a) meets these requirements. But see also

In brief, each of the mechanisms for the elimination of microorganisms recited in the Casey and Coates references are distinguishable from the specific pH level and specific level of alcohol taught by the present applicant's specification with regard to antimicrobial efficacy. Casey teaches that its antimicrobial efficacy arises from its recited "surfactant-detergent compounds", and that the role of pH is relevant only to ensuring the de-colorization of its pH sensitive dyestuff. Casey is wholly silent however as to any efficacy against the microorganisms recited in prior claim 22 as well as specifically claimed in newly presented claim 23, and absent such a teaching such efficacy cannot be presumed. Such is well recognized in the literature. The Coates compositions clearly define that a combination of a bisguanide antimicrobial agent with a quaternary ammonium antimicrobial agent provides its antimicrobial efficacy against several microorganisms. Coates is also silent however, as to any efficacy against the polio virus as well as the further specific microorganisms recited in many of applicant's presently amended claims and absent such a teaching such efficacy cannot be presumed. Indeed, from the literature, the opposite is propertly presumed. Any combination of the Coates and Casey references would require that the resultant compositions necessarily include Casey's essential recited "surfactant-detergent compounds" additionally in conjunction with Coates' essential combinations of a bisguanide antimicrobial agent with a quaternary ammonium antimicrobial agent provides its antimicrobial efficacy, which would result in an "antimicrobial cocktail" of sorts in order to provide antimicrobial

efficacy against a limited number of microorganisms. Such however would not recognize or suggest any antimicrobial efficacy against each of *Entercoccus hirae* , *Aspergillus niger, T. mentagrophytes,* Hepatitis A , Poliovirus Type 1, Coxsachievirus , Rotavirus, or Rhinovirus by the applicant's three essential constituents, viz., "system", whose necessary constituents include water, a alcohol constituent selected from the group consisting of methanol, ethanol, n-propanol, isopropanol, n-butanol, benzyl alcohol, and mixtures thereof (but preferably ethanol, isopropanol or mixtures thereof, but especially preferably where the sole alcohol constituent is ethanol) and a pH adjusting agent.

Accordingly, in view of the foregoing remarks, reconsideration of the propriety of the rejection under 35 USC 103(a) is requested, and it is further requested that the rejection be withdrawn.

Should the Examiner in charge of this application believe that telephonic communication with the undersigned would meaningfully advance the prosecution of this application, they are invited to call the undersigned at their earliest convenience.

PETITION FOR A TWO-MONTH EXTENSION OF TIME

The applicants respectfully petition for a two-month extension of time in order to permit for the timely entry of this response. The Commissioner is hereby authorized to charge the fee to Deposit Account No. 14-1263 with respect to this petition.

CONDITIONAL AUTHORIZATION FOR FEES

Should any further fee be required by the Commissioner in order to permit the timely entry of this paper, inclusive of the fee for the accompanying *RCE*, the Commissioner is authorized to charge any such fee to Deposit Account No. 14-1263.

Respectfully Submitted;

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CERTIFICATION OF TELEFAX TRANSMISSION:

I hereby certify that this paper and all attachments thereto is being telefax transmitted to the US Patent and Trademark Office to telefax number: 571 273-8300 on the date shown below:

Andrew N. Parfomak — Date: 01 Nov 2007

Enclosures –

1) excerpt from "Disinfection, Sterilization and Preservation" 5th. Ed. Seymour S. Block, PhD (Editor) (2001) - 3 sheets

2) "Author Letter: " – 1 sheet

3) "Should the Test Methods for Efficacy of Disinfectants use Vertebrate Viruses Dried on Carriers to Advance Virucidal Claims Substantiation in Public Health Arena", by Dr. M. Khalid Ijaz and Joseph Rubino – 7 sheets

4) Request for Continued Examination (RCE) Transmittal – 1 sheet

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Disinfection, Sterilization, and Preservation

Fifth Edition

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LIPPINCOTT WILLIAMS & WILKINS
A Wolters Kluwer Company
Philadelphia • Baltimore • New York • London
Buenos Aires • Hong Kong • Sydney • Tokyo

Acquisitions Editor: Jonathan W. Pine, Jr.
Developmental Editor: Joyce A. Murphy
Production Editor: Thomas Boyce/Jonathan Geffner
Manufacturing Manager: Benjamin Rivera
Cover Designer: Christine Jenny
Compositor: Lippincott Williams & Wilkins Desktop Division
Printer: Courier Westford

530 Walnut Street
Philadelphia, PA 19106 USA
LWW.com

Printed in the USA

Library of Congress Cataloging-in-Publication Data

Disinfection, sterilization, and preservation / editor, Seymour S. Block.– 5th ed.
p. cm.
Includes bibliographical references and index.
ISBN 0-683-30740-1
1. Disinfection and disinfectants. 2. Antiseptics. 3. Sterilization. I. Block, Seymour Stanton, 1918–

RA761 .L33 2000
614.4'8–dc21 00-041221

10 9 8 7 6 5 4 3 2 1

isms such as polio, tuberculosis (TB), and spores is sound, but the bifurcation into "high" and "low" and the elimination of the category of "intermediate" implies to the practitioner either "good" or "bad." Perhaps the terms *broad spectrum, moderate spectrum,* and *narrow spectrum* may be more descriptive of the usefulness of these agents. After all, penicillin, which inhibits essentially only cocci and *Treponema* and not the dozens of gram-negative rods, TB, yeasts, molds, and viruses, is certainly not a low-level antibiotic. Antimicrobial designations, whether for disinfectants or for chemotherapeutics, should be based on common principles of nomenclature.

SCALE OF SUSCEPTIBILITY

Table 28.5 is an approximate disinfection scale for all the categories of microorganisms likely to be encountered in medical and veterinary environments. Reference to this chart can help in making sensible decisions about which disinfectant to use in a particular situation. When fecal contamination is likely (possible rotavirus or Coxsackie virus), a disinfectant with a rhinovirus claim (common cold) would be superior to one with only a TB claim. This table makes it clear that a knowledge of the spectra and modes of action of chemical agents can aid in the rational selection of disinfectant agents. Thus, for example, if a hospital disinfectant kills *Staphylococcus aureus,* it is clearly capable of inactivating practically all agents in susceptibility group A, that is, common (but not all) gram-negative rods as well as lipophilic viruses such as influenza and herpes. If a disinfectant is capable of passing the EPA virucide test against poliovirus or a rhinovirus (the most difficult of the common infectious disease agents to inactivate by the EPA test within 10 minutes), little doubt exists that it is truly a broad-spectrum disinfectant in terms of susceptibility groups A, B, C, and D. HHBV is placed in group A based on the work of Prince et al. (1993) with QACs in chimpanzees.

Still, it can be difficult to predict the activity of a formulation (as opposed to a pure "active") because various ratios of excipients, sequestrates, solvents, detergents, and actives produce nonspecific and synergistic effects. For example, the presence of alcohol, detergents, and wetting agents will enhance all virucidal claims. Formulations containing QACs are generally less active against enteroviruses and adenoviruses (compared with their antibacterial effect) than are formulations containing phenolics, aldehydes, or halogens. Most hospital disinfectants, whether they contain iodophors, phenolics, or QACs, are equally effective against lipophilic viruses such as influenza, acquired immunodeficiency syndrome (AIDS), and herpes. The benefits of QACs in hospitals are generally underestimated because they lack activity against TB in endoscopic procedures. Putting this aside, they are truly broad spectrum and biodegradable and are relatively nontoxic, making them extremely important environmental germicides. Their rate of kill is exceptionally fast.

TABLE 28.5. *Approximate disinfection scale for all organisms in order of increasing resistance (response to commercial disinfectants)*

Microbial susceptibility group[a]	Microorganisms (dried on carriers)
A	Retroviruses (AIDS), ortho and paramyxoviruses, herpes viruses, vaccinia, corona, other enveloped viruses, gram-negative rods and some filamentous fungi; some gram-positive cocci, human hepatitis B virus
B	*Staphylococcus aureus;* some diphasic and filamentous fungi, yeasts and algae, some gram-negative rods
C	Adenoviruses
D	Mycobacterium tuberculosis (BCG strain)[b] rotaviruses, reoviruses, some mold ascospores
E	Picornaviruses (polio, rhino) Parvoviruses (SS DNA), hepatitis A
F	Bacterial endospores *(Bacillus, Clostridium);* viroids
G	Prions (chronic infectious neuropathic agents, slow viruses)

[a]Exceptions will be found to exist among and between the various susceptibility groups listed, but the broad outline of comparative susceptibility has become a basic principle in disinfectant biology.

[b]Unfortunately little information is available on human strains, such as H37Ra, H37Rv, the various scotochromogens, drug-resistant forms, *Mycobacterium avium* intracellulare, and species of *M. fortuitum* and *M. chelonii* as well as pathogenic actinomycetes.

AIDS, acquired immunodeficiency syndrome; BCG, bacille Calmette-Guérin.

MECHANISM OF ACTION

All the agents listed in Table 28.4 can be classified into three groups based on mechanism of action, as set forth in Table 28.6, which describes the denaturing, reacting, or oxidizing properties of most disinfectants.

The QACs and phenolics are highly effective against lipophilic viruses. QACs as pure substances have the advantage of detergency, and at the use-dilution they possess little to no toxicity; in limited concentrations, they can be used for food contact surfaces.

The mechanism of action of other virucidal agents is shown in Table 28.7. These agents, representing a variety of chemical and physical techniques, inactivate viruses for the most part by means of a covalent reactant pathway. It should be made clear that these agents, as well as all disinfectants, "inactivate" viruses by disrupting their surface structures. Antibacterial activity, on the other hand,

View Final Author Letter

MS Title:	**SHOULD THE TEST METHODS FOR EFFICACY OF DISINFECTANTS USE VERTEBRATE VIRUSES DRIED ON CARRIERS TO ADVANCE VIRUCIDAL CLAIMS SUBSTANTIATION IN PUBLIC HEALTH ARENA?**
MS Number:	ICHE-2007-307 Version 3
MS Type:	Letter to the Editor
Section:	No section assigned.

Author Letter:

Dear Dr. Ijaz:

I am pleased to inform you that your manuscript, "SHOULD THE TEST METHODS FOR EFFICACY OF DISINFECTANTS USE VERTEBRATE VIRUSES DRIED ON CARRIERS TO ADVANCE VIRUCIDAL CLAIMS SUBSTANTIATION IN PUBLIC HEALTH ARENA?," has been accepted for publication in Infection Control and Hospital Epidemiology.

Before publication, you will receive page proofs, along with a form to order reprints, from the University of Chicago Press, who is the publisher of the journal. Your manuscript will be edited for style, clarity, and length. You will be notified by e-mail when the proofs are ready. Please return the corrected proofs promptly to avoid a delay in publication.

We look forward to working with you during the remainder of the publication process. Thank you for your interest in Infection Control and Hospital Epidemiology.

Sincerely,
Suzanne F. Bradley, MD
Editor-in-Chief

SHOULD THE TEST METHODS FOR EFFICACY OF DISINFECTANTS USE VERTEBRATE VIRUSES DRIED ON CARRIERS TO ADVANCE VIRUCIDAL CLAIMS SUBSTANTIATION IN PUBLIC HEALTH ARENA?

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TEST METHODS FOR MAKING VIRUCIDAL CLAIMS

TO THE EDITOR - The advancements made in the past decade in microbicidal science have raised questions to the appropriateness of test methods still being used to substantiate microbicidal and virucidal claims globally. The test methods currently being used for evaluation of virucidal activity of disinfectants employ the challenge virus either dried on prototypical hard surfaces or in suspension. The latter approach presents a weaker challenge to the formulation under test .[1,2] Regulatory agencies such as the U.S. EPA, Canadian General Standard Board (CGSB) and Australian Therapeutic Goods Administration (TGA) require data for virucidal activity based on carrier test methods using vertebrate viruses.[3-6] In contrast, European methods (both BS EN 14476:2005 and EN 13610) for virucidal activity not only use suspension tests but EN 13610 employs bacteriophages as opposed to vertebrate viruses for making claims in the public health arena. [7, 8] We believe that both of these European methods are unrealistic and do not represent field situations where disinfectants are used for decontamination of pathogens dried on hard surfaces in domestic, health care or extended care settings. In this letter, our comments on the irrelevancy of both (BS EN 14476:2005; EN 13610:1999) of these standards are based on our experience of over twenty years as manufacturers of microbicidal products and also developers of methods for virucidal activity of disinfectants. A number of our carrier test methods have been approved by the US EPA to generate virucidal data for product registration. [3] Such virucidal data are also accepted by CGSB, TGA and jurisdictions in Asian countries as well. [5, 6]

TEST METHODS FOR MAKING VIRUCIDAL CLAIMS

Vertebrate viruses and *not* bacteriophages on naturally-contaminated environmental surfaces pose a danger to public health. Disinfectants with demonstrated virucidal activity against these pathogenic viruses play a pivotal role in the interruption of viral dissemination through such vehicles. Experts believe that ideal disinfectants should be effective against both Gram-positive and Gram-negative bacteria as well as pathogenic viruses when tested using carrier-based test methods.[1, 2, 10]

Scientific literature strongly support that data generated using relevant vertebrate viruses such as enteric (coronavirus, rotavirus) or respiratory (influenzaviruses, rhinovirus) viruses are relevant to real life situations and should be considered for issuing relevant virucidal claims. It is therefore of paramount importance to consider the following for product registrations making virucidal claims:

1. Vertebrate viruses (not bacteriophages) are emerging / re-emerging pathogens of public health concern.
2. Vertebrate viruses survive on contaminated environmental surfaces which may play a role in infectious virus dissemination.
3. Virucidal test methods employing viruses dried on prototypical environmental surfaces are more challenging to disinfectants than viruses in suspension as required by EN 13610:1999 or BS EN 14476:2005.

4. Antimicrobial test methodologies development organizations such as ASTM International have developed virucidal testing parameters which include vertebrate viruses (enveloped and naked / non-enveloped viruses).
5. The EN 13610:1999 or BS EN 14476:2005 requiring virucidal testing against only bacteriophages or non-enveloped vertebrate viruses will eliminate many disinfectants otherwise effective against emerging and re-emerging viruses.
6. Regulatory agencies worldwide (U.S., Canada and Australia including Asians) accept virucidal efficacy data generated using vertebrate viruses (enveloped or naked / non-enveloped viruses). This is in line with consumer and infection control community's demand to know the virucidal efficacy of the products to use in emerging / re-emerging pathogen situations such as SARS-HCoV, avian influenza virus and recently rabies in China and bat-borne Melaka virus, a type of reovirus in Malaysia
7. Public health agencies such as Center for Disease Control and Prevention (CDC) in the U.S. as well the WHO issue public advisories in emerging pathogen situations based on claims registered products make against vertebrate viruses.

Therefore, it is scientifically justifiable to use vertebrate viruses (enveloped or non-enveloped viruses) to generate virucidal efficacy data for making relevant virucidal claims which add value to and place greater confidence in any virucidal claim both in the minds of infection control community and public at large (Figure). If only the naked / non-enveloped bacteriophages or viruses are used for virucidal testing in suspension as required by EN 13610:1999 or BS EN 14476:2005, it is not only irrelevant to field

situations, it will force the manufacturers of disinfectants to over formulate or use more potentially toxic ingredients due to challenging virucidal hierarchy of naked viruses (non-enveloped vertebrate viruses or bacteriophages).

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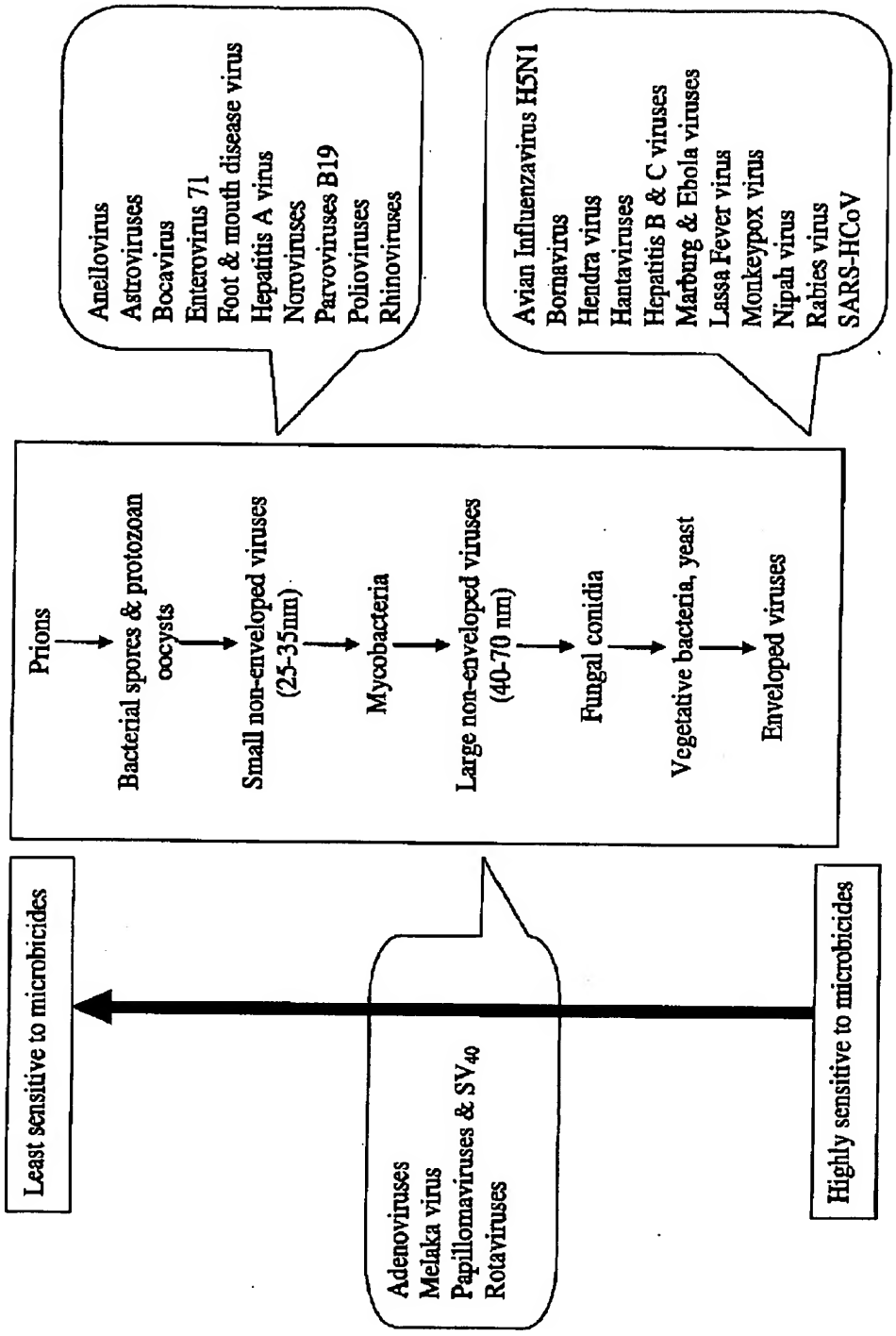

Figure : Emerging / re-emerging viruses and microbicidal hierarchy.